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Moringa Oleifera Seed Oil Modulates Effects of Acetaminophen on Some Biochemical Parameters in Male Rats

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Abstract

Moringa oleifera (MO) is a common herbal plant used as human food and for medicinal purposes worldwide. Acetaminophen (APAP) is used as antipyretic and analgesic drug, while causing hepatotoxicity at over dose.The present study is aimed to evaluate the hepatoprotective effect of MO seed oil extract against the biochemical changes induced by APAP in male adult albino rats. Thirty five male albino rats were used in this study, divided randomly into five groups (7 rats in each). The 1st control group; untreated animals, the 2nd saline group received single dose of normal physiological saline, the 3 rd group treated with single dose of APAP (500 mg / kg b.wt) for hepatotoxicity induction, the 4th group treated with MO seed oil extract (0.3 ml/rat) daily for 30 days and the 5th group treated with a single dose of APAP and with MO seed oil extract daily for 30 days to evaluate its protective effects. Blood samples were collected for serum preparation and biochemical analysis. Results showed that APAP induced a significant increase in blood glucose level which is against to the effect produced by the treatment with MO seed oil. All measured kidney function parameters increased significantly after treatment with APAP. Oppositely, animals treated with MO seed oil after APAP showed depression in kidney function parameters. APAP treated group showed significant decreases in catalase (CAT) activity and reduced glutathione (GSH) level while showed a significant increase in malondialdehyde (MDA) activity. Rats treated with MO seed oil showed significant increases in catalase and GSH activities while caused a significant decrease in MDA concentration. Treatment with MO seed oil after APAP induced significant decrease and increase in GSH and MDA levels respectively compared to those of control group. The present study concluded that the MO seed oil extract has ameliorative effects against some biochemical disturbances induced by acetaminophen possibly through its anti-oxidative properties.

Keywords: Acetaminophen, Moringa oleifera, Antioxidant enzymes, Kidney functions.

1. Introduction

At ancient times medicinal plants were used for the treatment or aliment of human disease. Nowadays, the industries which based on medicinal plants as therapeutics for human and animal diseases increase throughout the world [1]

Moringa oleifera is one of the most important natural plants which used as herbal medicine. It belongs to family Moringacea which its diverse parts have been employed as food and medicine [1]. Several health benefits were reported as a result of supplementations of Moringa leaves and seeds or their extracts [2].

Seed oil of Moringa oleifera (also known as Ben oil) used in many purposes as nutrition, manufacture of perfume, hair care products and treatment of many diseases such as rheumatism. Ben oil has anti-oxidation activity and significant protection against chemical-induced liver injury, so it has been used in liver disorders by folk medicine practitioners [3].

Analysis of MO seed oil has shown its high content of α, γ and δ-tochopherols and high content of sterols such as (β-sitosterol and fatty acids) which act as anti-oxidant and free radical scavengers [3,4].

The present study aimed to evaluate the possible ameliorative effect of Moringa oleifera seed oil extract against acetaminophen-induced biochemical and physiological disturbances in the liver of Wister albino rats.

2. Material and methods

2.1 Hepatotoxic agent

Acetaminophen (APAP) a white or almost white, crystalline powder, sparingly soluble in water was purchased from Zhejiang Kangle Pharmaceutical CO., (China)

2.2 Plant

Moringa olifera (MO) seed oil used in this study was obtained from Egyptian Scientific Society for Moringa - National Center for Research, Giza, Egypt. Seed oil obtained by cold press of seeds, using simple hydraulic hand press [5].

2.3 Experimental animals

Thirty five male albino rats; Rattus norvegicus weighting 175± 10 were purchased from Helwan Farm of Egyptian Organization for Vaccines and Biological Preparations. Animals were housed in a clean cage under laboratory condition (temperature 25±2°C with dark/light cycle 12/12h) for 10 days before the beginning of the experiment. Animals were allowed to food and tap water adlibitum.

2.4 Experimental design

Rats were divided randomly into five groups consisting of 7 animals in each group. Normal untreated rats (control group):, animals received single dose of normal physiological saline (saline group), animals received one dose of 500mg/kg b.wt APAP dissolved in saline, (APAP group), animals received one daily dose of 0.3 ml/rat Moringa olifera seed oil for 30 days (MO Group) and rats received one dose of 500mg/kg b.wt.

APAP dissolved in0.5ml saline then 0.3 ml/rat MO seed oil extract daily for 30 days (APAP + MO group).

2.5 Blood sampling

All treatments administered using intragastric tube. At the end of the experiment; the animals were fasted for 12 hours then anaesthetized using diethyl ether inhalation **[6]**. Blood samples were collected from post caval vein of each rat, collected in dry centrifuge tubes and centrifuged at 3000 rpm for 15 min. Then sera were separated and frozen at -20 °C until usage for biochemical analysis. All Parameters were determined using 5010 spectrophotometer, model: 7315 made in Germany .

2.6 Measurements

a) Blood glucose (mg / dl)

Blood glucose level was determined by the enzymatic colorimetric method according to [7] using Biodiagnostic reagents.

b) Kidney function parameters

By using Biodiagnostic reagents serum urea, uric acid and creatinine levels were determined by enzymatic colorimetric methods according to [8, 9, 10] respectively.

Blood urea nitrogen (BUN) was calculated according to [11]. by the equation: BUN = Urea×0.460.

c) Anti-oxidant parameters

Serum Malandialdehyde, reduced glutathione and catalase activity were determined by colorimetric method using Sigma Aldrich reagents according to [12, 13, 14] respectively.

2.7 Statistical Analysis

The value of each measured and calculated parameters were expressed as the mean of 7 individual values ± standard deviation "SD" .The results obtained were evaluated using one way analysis of variance ANOVA test at ($P \leq 0.05$) according to [15], on Statistical program for Social Sciences (SPSS) Version 20 was used.

3. Results and discussion

3.1 Blood glucose

Blood Glucose level of rats treated with saline decreased significantly compared to those of control group. The treatment of rats with 500mg/Kg APAP caused significant increase in blood glucose level as compared to that of control group and other treated groups. Blood glucose level in rats treated with MO seed oil and in those treated with APAP then MO seed oil decreased significantly as compared to control and other treated groups Table (1).

Glucose is a major fuel for animal cells .It is supplied to the organ through dietary carbohydrates and endogenously, through hepatic gluconeogenesis and glycogenolysis. Glucose absorption from the gastro intestinal tract into blood is regulated by a variety of neuronal signals and entero hormones, as well as by meal composition and the intestinal flora. Glucose homeostasis reflects a balance between glucose supply and its utilization [16]. In our study, serum glucose level was increased in APAP hepatotoxic rats. This is in agreement with [17] who demonstrated that glucose level was significantly increased in APAP hepatotoxic female albino rats.

The results of the present study showed that treatments with Moringa oleifera seed oil induced a significant decrease in serum blood glucose level compared with that of APAP hepatotoxic rats. This may be due to the antioxidants like carotenoids, vitamins C and E, and flavonoid constituents of MO which had an important role in reducing the blood glucose [18]. Or this may due to an improvement in glucose metabolism and a decrease in insulin resistance [19]. Our result correlated with those of [20] and with [21] who demonstrated the reduction in blood glucose level in rats treated with Moringa oleifera ethanol leaf extract due to presence of phytomolecules, (including polyphenols, flavonoids, lycopene, and ß-carotenes), stilbeans, glycoside and alkaloids in Moringa oleifera and other bio active compound which has anti –diabetic effect by causing an increase in insulin output or by inhibition of the intestinal glucose absorption.

3.2 Kidney function parameters

The results presented in Table (2) revealed that rats treated with saline showed non-significant differences in uric acid and creatinine levels from those of control group, while showed significant increases in levels of urea and blood urea nitrogen compared to those of control one. Treatment with APAP caused significant increase in all measured kidney function parameters (uric acid, urea, blood urea nitrogen and creatinine) as compared to control and other treated groups. The administration of MO seed oil significantly decreased all measured kidney function parameters, when compared to the control and other treated groups. All measured kidney function parameters increased and decreased significantly in last group of APAP then MO seed oil as compared to all groups and APAP treated group, respectively. Renal toxicity caused by APAP is closely related to its metabolism in liver, due to the metabolism of cytochrome P450 enzyme system which produces N-Acetyl-P-benzoquinone immine "NAPQI" that is toxic to the liver and kidney and this leading to depletion of GSH level with increase in lipid peroxidation level and consequent induction of tubular necrosis which were confirmed by the current results [22, 23] Also, in the current study acetaminophen induced increasing of serum urea, creatinin and uric acid levels. This was in agreement with [24] who said that acetaminophen promote the increment in urea and creatinin level leading to uremaia. Also these results were in agreement with those of [25] who mention that administration of nephrotoxic dose of acetaminophen to rats resulted in significant elevation of serum levels of urea, creatinin and uric acid.

Moringa oleifera ameliorate the effect of acetaminophen induced kidney damage. This effect may be attributed to its fatty acid content or to the presence of protective antioxidants [26]. So Moringa oleifera prevented the elevation of the indices for renal dysfunction [27] These results were in agreement with those [28, 29] The authors

demonstrated that treatment with Moringa oleifera reduced the level of serum urea and creatinin, and also mentioned that Moringa oleifera at high concentration improved the nutritional value and realized the best effect on kidney function. This could be due to the anti-inflammatory and antioxidant activities of the Moringa oleifera which had been shown to be attributable to the presence of polyphenols and tannins [30].

3.3 Anti-oxidants

Table (3) indicated, statically that saline administration caused non-significant differences in all measured anti-oxidant Catalase (CAT), reduced glutathione (GSH) and malondialdehyde (MDA), activities compared to those of control group. As compared to control and treated group, APAP group showed significant decreases in catalase activity and reduced glutathione while showed significant increase in MDA activity. The administration of MO seed oil caused significant increase in catalase and reduced glutathione activities while caused significant decrease in MDA activity when compared to control and other treated groups. Rats treated with MO seed oil after APAP showed non-significant change in catalase activity compared to those of control and saline groups, but showed a significant increase and decrease compared to APAP and MO seed oil treated groups respectively. The activities of reduced glutathione and MDA decreased and increased significantly in 5th group compared to those of control group, which is in contrast with the results revealed by comparison to APAP treated group Table (3)

Acetaminophen intoxication increases reactive oxygen species and reactive nitrogen species which emerged as potential secondary mediators involved in cell death, this may induce oxidative damage to all type of cellular macromolecules [31]. Additionally, APAP caused significant increase in hepatic lipid peroxidation due to free radical injury in necrotic livers of rats [32]. In our results APAP caused significant decreases in catalase and reduced glutathione activities while caused significant increase in MDA activity, that clear manifestation of excessive formation of free radicals and activation of lipid peroxidation system resulting in tissue damage. These results in harmony with those of [33] who reported that administration of APAP induced a significant decrease in CAT activity and elicited a significant increase in MDA level. Also [34] demonstrated that there were decreases in levels of GSH and catalase activities, and increases in serum marker enzymes and lipid peroxidation level in APAP treated rats which may be due to hepatocellular damage. Glutathione, the most abundant tripeptide thiol, is the endogenous non-enzymatic antioxidant in our body system and it is a protective against chemically induced hepatic damage and oxidative stress [35]. GSH removes free radical species such as hydrogen peroxide, superoxide radicals and maintains membrane protein thiols. The GSH depletion in hepatic mitochondria is considered the most important mechanism in the APAP induced hepatotoxicity. Reduced GSH level was depleted in APAP treated rats may be due to conjugation of GSH with NAPQI to form mercapturic acid. [34]. Catalase (CAT) is a haem containing enzyme catalyzing the detoxification of (hydrogen peroxide H2O2) to water and oxygen [36]. Catalase converts harmful hydrogen peroxide into water and oxygen and protects the tissues from highly reactive hydroxyl radicals. The reduction in the activity of this enzyme may results in a number of deleterious effects due to accumulation of highly toxic metabolites and hydrogen peroxide by APAP administration [34].The previous data explains the toxic effect of APAP& oppositely the protective role of MO in our experiment.

Moringa oleifera has a property of inhibition of lipid peroxide formation by scavenging of free radicals. The antioxidant property of Moringa may be due to the presence of phenolic compounds Moringa oleifera may be a good inhibitor of drug-induced oxidative stress , as Moringa oleifera rich in β-carotene which may be exhibit a good radical trapping anti-oxidant activity [37] In our study, Moringa oleifera seed oil cause improvement in anti-oxidant activity of rats as it caused significant increases in catalase (CAT) and reduced glutathione activities while showed significant decrease in MDA activity. This with agreement with [3] who mention that analysis of the Moringa oleifera seed oil has shown a considerable antioxidative activity β-carotene tests and suggested that the tocopherols and other unknown antioxidant components as well as unsaturated fatty acids in the oil might contribute to free radical scavenging property and inhibit the chain reaction of lipid peroxidation. β-carotene, and vitamins A and C present in Moringa oleifera serve as anti-oxidant component [18]. Our result also agreed with [2] who mention that the antioxidant activity of Moringa seed powder is due to its content of phenolics and flavonoids that have scavenging effect on the free radicals.

Table (1) Effect of"' Moring olifera "MO" seed oil"(0.3g/rat daily for 30 days) on blood glucose level of rats.

Groups / Parameters	Control	saline	APAP	MO	APAP +MO
Glucose (mg/dl)	105.30± 2.80^{b}	99.80± 3.43^{c}	121.20±2.06^{a}	82.10 ± 1.98^{d}	49.40±2.14e

Treated with a single dose of acetaminophen "APAP" (500 mg/k.g .b.wt) by intragastric tube
All data expressed as mean ±SD for 7 rats.
a, b, c, d = values in the same row with different letters are significantly different ($P < 0.05$)

Table (2) Effect of"' Moring olifera "MO" seed oil"(0.3g/rat daily for 30 days) on" Serum urea , uric acid, creatinine and blood urea nitrogen (BUN) levels" of rats treated with a single dose of acetaminophen "APAP" (500 mg/K.g .b.wt) by intragastric tube.

Groups / Parameters	Control	saline	APAP	MO	APAP +MO
Urea (mg/dl)	39.00±1.33^{d}	41.14±0.65^{c}	61.27±1.01^{a}	32.88±0.30^{e}	43.32±1.78^{b}
Uric acid (mg/dl)	2.08±0.18^{c}	2.10±0.16^{c}	5.67±0.33^{a}	1.90±0.29^{c}	4.52±0.38^{b}
Creatinine (mg/dl)	0.39±0.01^{c}	0.40±0.01^{c}	1.20±0.16^{a}	0.12±0.08^{d}	0.79±0.08^{b}
BUN (mg/dl)	17.92±0.59^{d}	18.93±0.28^{c}	28.20±0.46^{a}	15.10±0.17^{e}	19.94±0.81^{b}

All data expressed as mean ±SD for 7 rats.
a, b, c, d = values in the same row with different letters are significantly different (P < 0.05).

Table (3) Effect of"' Moring olifera "MO" seed oil"(0.3g/rat daily for 30 days) on "Catalase (CAT), Reduced glutathione (GSH) and melandeoldhyde (MDA) of rats treated with a single dose of acetaminophen "APAP" (500 mg/K.g .b.wt) by intragastric tube.

Groups / Parameters	Control	Saline	APAP	MO	APAP +MO
Catalase (U/L)	48.50±1.91^{b}	48.50±2.38^{b}	34.25±2.87^{c}	85.00±3.55^{a}	45.50±1.73^{b}
GR (U/L)	145.00±2.44^{b}	143.75±2.62^{b}	131.5±2.64^{d}	166.75±2.36^{a}	139.25±2.98^{c}
MDH (nmol/ml)	153.00±2.16^{c}	151.75±2.36^{c}	219.50±4.20^{a}	139.25±2.50^{d}	195.00±4.08^{b}

All data expressed as mean ±SD for 7 rats.
a, b, c, d = values in the same row with different letters are significantly different (P < 0.05).

4. Conclusion

The present study concluded that the Moringa oleifera seed oil extract has ameliorative effects against some biochemical disturbances induced by acetaminophen possibly through its anti-oxidative properties. and inhibiting oxidative stress induced damage.

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